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VASCULAR DISEASE

ENHANCED ANTIANGIOGENIC EFFICACY OF PRODRUG NANOPARTICLES QUANTIFIED WITH MAGNETIC RESONANCE IMAGING

ACC Poster Contributions
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Tuesday, April 05, 2011, 9:30 a.m.-10:45 a.m.

Session Title: Vascular --Pathophysiology -- Basic/Angiogenesis/Gene Therapy
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Background: αvβ3-fumagillin nanoparticles (NP) decrease angiogenesis in atherosclerotic rabbit models, but drug losses from NPs in circulation and chemical instability of fumagillin complicate translation. To develop a prodrug (PD) platform for improved chemical and circulatory stability of drugs in lipid-based NPs.

Methods: PD of fumagillin was coupled to the Sn-2 acyl position of phosphatidylcholine, which included removal of fumagillin light sensitivity. PD were formulated in perfluorocarbon NPs and studied in 2F2B endothelial cell proliferation assays. Efficacy of αvβ3-fumagillin-PD NP, nontargeted-fumagillin-PD NP, αvβ3-fumagillin NP and αvβ3-no drug NP were studied in a Matrigel mouse angiogenesis model. Mice (N=6/grp) were treated on days 6, 9, and 12 post-implantation and neovascularity imaged on day 16 with MRI and αvβ3-paramagnetic NP.

Results: αvβ3-PD NPs decreased ($p<0.05$) cell proliferation equal or better than equi-molar doses of free drug. αvβ3-fumagillin-PD NP decreased ($p<0.05$) Matrigel angiogenesis; no effects were measured in the other groups.

Conclusions: Sn-2 fumagillin PD offer improved chemical and circulatory stability in lipid-based NPs, facilitating translation of NP-based antiangiogenic treatment for atherosclerosis.